# Editorials

## The Problem of Methamphetamine Toxicity

THE TWO ARTICLES on methamphetamine in this issue draw attention to an important fact: We know very little about this drug. Most of what we do know comes from the Japanese literature and a handful of published case reports. But generalizing from case reports is unreliable, and the experience of other cultures may not apply to ours. Methamphetamine has been a major problem in Japan since the end of World War II,[1] but in the United States the overall prevalence of methamphetamine misuse has remained modest, especially when compared to cocaine.

In the 1996 report of the Drug Abuse Warning Network (DAWN), 4,462 deaths were attributed to cocaine compared to only 487 for methamphetamine, roughly a 10 to 1 ratio.[2] Preliminary results for 1997 suggest little change. Emergency room visits have nearly doubled, however, from the first half of 1996 to the first half of 1997 (from 4,200 to 8,400). There were 80,000 cocaine-related visits during that same period.[3] Unlike cocaine, which is a major problem everywhere in this country, methamphetamine misuse remains less common. Since 1991, not a single death from methamphetamine misuse has been reported in Atlanta, Baltimore, Boston, Buffalo, Miami, or Newark.

The demographics of this drug raise some fascinating questions about mechanisms of toxicity. DAWN statistics for 1997 indicate that more than half the emergency room visits were by people under age 35 (4,482/8,316) and that a third of the visits to emergency rooms due to methamphetamine misuse were by women (2,983/8,316). In autopsy studies, however, the mean age of decedents is closer to 38 years, many are in their 40s and 50s, and almost all are men. This is consistent with the results of successive National Household Surveys on drug misuse. That instrument continues to show that the population of drug misusers is aging. In 1979, when the survey first began, only 10% of misusers were over age 35. The percentage has now increased to nearly a third.[4] This age disparity raises the possibility that methamphetamine-related deaths may have a long incubation period. Typical findings at autopsy include multivessel coronary artery disease and myocardial hypertrophy.[5] Aortic dissection is also more common than is generally appreciated. Multivessel coronary artery disease does not develop overnight, and neither does myocardial hypertrophy or medial degeneration. The evidence suggests that most methamphetamine users die of chronic, not acute, toxicity. The full extent of the problem may not be apparent for several more years.

Today, most journal editors would reject a paper on myocardial infarction related to cocaine misuse on the grounds that the disorder is so common that it is no longer reportable. Yet only a handful of reports describe infarction in methamphetamine misusers. The explanation may have to do with the production of heat-shock protein. In experimental animals, amphetamines can increase levels of the inducible heat-shock proteins. These are a group of cellular homeostatic proteins induced in vascular tissue by catecholamines.[6] Cocaine does not appear to be as effective an inducer of heat-shock protein as methamphetamine. It may be that methamphetamine misusers benefit from a degree of myocardial protection that cocaine misusers do not.

Many other questions remain to be answered; but because complications from methamphetamine misuse are uncommon, these answers will be hard to come by. Environmental exposure to drugs is a reality. Cocaine, for example, can be detected in most circulating currency.[7] A few years ago, in California, a mother was charged with murder by breast feeding when a few nanograms of methamphetamine where detected in her dead son. The child also had viral pneumonia and pericarditis.[8] The detection of trace quantities of a drug only proves that the drug is in the environment, not that it has caused any particular syndrome. Even very substantial amounts of drug may represent nothing more than an incidental finding.[9] Great care must be taken not to needlessly exaggerate the threat by extrapolating too much from isolated case reports.

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